Senn. (N.)

Importance and Value

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Experimental Research

DOCTORATE ADDRESS

DELIVERED AT THE GRADUATING EXERCISES OF THE COLLLEGE OF PHYSICIANS AND SURGEONS, CHICAGO, ILL., FEB. 21, 1887.

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N. SENN, M. D., Milwaukee, Wis.

Professor of Principles and Practice of Surgery and Clinical Surgery.

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A Doctorate Address delivered at the Fifth Annual Commencement Exercises of the College of Physicians and Surgeons, Chicago, Feb. 21, 1887.

GENTLEMEN OF THE GRADUATING CLASS:—To-day marks a new era in your lives. The time you have been so anxiously awaiting has arrived. The dreams of your youth are realized. You have left the college building where you spent so many days in acquiring a knowledge of the healing art, and in recognition of work well done you have just been received into the ranks of a great and noble profession. The pleasant relations which have existed between us as teachers and students have come to a close. As teachers we congratulate you, as colleagues we welcome you and extend to you the right hand of fellowship. With parental solicitude we shall follow you into the arena of active professional life, fully confident that every one of you will meet with well merited success.

An honorable struggle for a remunerative practice is justifiable and desirable, but a successful career is not always to be measured by weight in gold. One of the great objects in life must be to become contributors to science. Even at the very threshold of your professional career you have incurred a heavy debt, in the payment of which some of the very best efforts of your lives will be required. During your pupilage you have enjoyed advantages that were not in reach of students even a few years ago. The progress made in medicine and surgery and the allied sciences during the last two decades is unparalleled in the history of medicine. One discovery has followed another until we have witnessed a complete revolution in the treatment of injuries and disease. Text-books of a few years ago that were then considered as standard authorities are now consigned to the shelves of the antiquarian, as the very principles upon which their teachings were based have undergone a radical change. You have been instructed in the most recent advances pertaining to your profession. You have been made familiar with both ancient and modern literature, and have thus derived the benefit resulting from the accumulation of knowledge which it has required centuries to develop. You owe to science a debt which can only be paid by faithful and persevering study and research, in enlarging its boundaries and in increasing its store of wealth. While you are no longer students under the supervision of teachers you should dedicate your future lives to the study and improvement of your chosen profession. We have inherited a trust which can only be invested profitably by hard, unselfish work. The study of medicine is inexhaustible and affords ample scope to occupy all your leisure moments. As teachers we have simply laid the founda-

tion for your medical education and must leave it to your own efforts and inclinations to complete the structure. Commence your life-work with a firm determination to continue your studies in a systematic manner. It is not only necessary for you to keep familiar with the current medical literature, but you should also strive to render material aid in the future growth and development of our science. A reward greater in value than gold, and more enduring than fame, is a consciousness of having contributed to the increase of knowledge.

With a view of pointing out to you the right direction in which such work can be accomplished, I have selected as the subject of my address, "The Importance and Value of Experimental Research." Experimental research implies the necessity of resorting to vivisection. It is not my intention to argue in justification of this method of investigation, as vivisections in original researches are performed only when questions in hand cannot be solved by any other method of study, and always with a definite object in view, and with this restriction no intelligent community has the moral right to interfere.

Modern medicine and surgery are founded upon a study of the organs of the body and their functions, that is, upon a knowledge—the more thorough the better—of the mechanism with which they have to deal. Empirical medicine and surgery have a foundation since they rest upon the observation of isolated facts, but the mere collection of information without reasoning upon it is useless, and many disconnected facts cannot construct a system capable of further development. A thorough knowledge of the structure of the body with which the physician and surgeon has to deal, the relations of its functions in health will enable him to act promptly and intelligently in case of injury or disease. Rational treatment is based upon sound physiology. Experimentation is part of a system,—the physiological system, and part of a method,—the experimental method. A scientific investigator is never a random experimenter. A comprehensive and accurate knowledge of the ancient and modern literature, and an intimate acquaintance with everything that is known relating to the subject is essential for successful work. As modern medicine and surgery are so intimately related to and associated with physiology, it is proper to ask: "What has experimental research done toward the development of the latter science?"

Erasistratus thought that the arteries contained air. Galen was a diligent experimenter, and his observations soon taught him that this was not the fact. He found that when an artery was cut blood escaped. He believed, however, that the arteries contained, besides blood, air or vital spirits, and that their function consisted in distributing this vivifying substance to the whole body. He was the first great experimental physiologist, and the knowledge derived from vivisection had elevated him to a position of prominence and influence which survived him for centuries. The physiology of the circulation after his time remained much in the same condition until the beginning of the 17th century. The great motor power of the heart was unknown to medical men of that time and the direction of the blood current through the vessels had not been ascertained. Practical observation at the bedside, and upon battlefields, had failed to familiarize the physician with the true mechanism of the circulation. The observations made upon living animals were directed more toward the study of anatomy than physiology. In the beginning of the

17th century Harvey followed the footsteps of Galen and laid the foundation for modern physiology by his discovery of the circulation. Malpighi and Leouwenhook, the founders of microscopical anatomy, were the first to observe the passage of the blood from the right to the left side of the heart through the pulmonary capillaries of a living frog by vivisection, thus adding the last link to Harvey's chain of evidence. Only a few years ago the researches of Waller and Cohnheim made on the circulation of the blood in lower animals have demonstrated the migration of white corpuscles through the capillary walls—a discovery which furnishes an adequate explanation of many pathological conditions, which, without it, would have remained shrouded in darkness.

Intracardiac pressure was first studied by Stephen Hales, who published his observations in 1732. The same subject, which of course could only be studied upon living animals, was investigated by Poiseuille, and more recently by Alfred W. Volkmann, who published the result of his researches in a large volume in 1850, entitled "Die Hæmodynamik nach Versuchen." As a result of these investigations a number of ingenious instruments, as the kymograph, sphygmograph, and cardiograph have been devised which have rendered material diagnostitial aid to the physician and surgeon, ascertaining the most delicate changes in the circulation, and are most valuable means in studying the fluctuations of disease. Haller, the great physiologist, demonstrated by his careful observations on living animals the independent muscular contractions in the arteries, a discovery fully confirmed by the experiments of Hunter and Thomson. Claude Bernard, Brown-Sequard and others established by experimentation the regulation of the blood supply to the various organs through the medium of the action of the nervous system upon the organs of circulation.

Gaspardus Asellius, a distinguished Italian anatomist, in 1662, while experimenting upon a dog which had just had a full meal, accidentally discovered the lacteal vessels which appeared as "a number of fine white cords," which he at first supposed to be nerves, but which, when punctured, proved to contain milky fluid. As at this time it was the general belief that the liver was the exclusive hæmato-genetic organ, he failed to search for the proximal termination of the lacteal vessels and entertained the belief that they terminated in the liver, an opinion which prevailed until Jean Pecquet, while experimenting for another purpose, discovered the thoracic duct, and by further research succeeded in tracing the general course and distribution of the lymphatic system.

The ancients entertained the most vague ideas in relation to the respiratory functions, believing that the air passed through the lung into the cavity of the chest, from there into the heart, where it came into direct contact with the blood. This opinion represented the whole knowledge upon this subject until the beginning of the 17th century, and was endorsed by such famous authorities as Harvey, Hall, and Boerhave. A series of experiments made by Haller demonstrated to the satisfaction of physiologists the mechanism of the respiratory function. Mayow, by experiment and logical induction, came to the conclusion that the atmospheric air was a compound, containing as one of its elements a body to which he assigned the properties possessed by oxygen, which from its supposed analogy to nitric acid he called nitro-aerial spirit. To this element of the air he attributed an active and essential part

in the process of combustion and respiration. Black, in 1759, showed by experiments the presence of carbonic acid in the expired air; and in 1770, Priestly proved by the same means the analogy of respiration to combustion, and asserted that atmospheric air in its passage through the pulmonary circulation lost some of its oxygen. Lavoisier's skillful and laborious experiments resulted in an accurate knowledge of the chemical changes which take place in the inspired air during the respiratory process. More recent experiments have determined almost with arithmetical precision the amount of oxygen consumed and carbonic acid exhaled by an individual during a specified time. Lower found when examining the open thorax of a living animal that the difference between the color of arterial and venous blood took place in the capillaries of the lungs and referred this phenomenon to a chemical change in the blood itself. The true explanation of this change was furnished by Priestly, whose experiments convinced the scientific world that the alteration was due to the purifying of the blood by means of the oxygen of the air. Our ancestors entertained a very peculiar idea concerning the complicated process which we now consider essential for healthy digestion and assimilation. The transformation of food into chyle was supposed to be effected entirely by the moisture and heat of the stomach producing a change which they termed "concoction." Then appeared the mechanical theory which advanced the idea that the mechanical division of food in the stomach by trituration constituted the most important part of digestion. Still later it was believed that the food introduced into the stomach underwent a process of putrefaction before it could be absorbed and utilized in the body.

Experimental research again had to come to the rescue of science to demonstrate the fallacy of all of these absurd doctrines. Spallanzani and Stephens showed that the mucous membrane of the stomach secreted a digestive fluid—the gastric juice—and made careful experiments to determine the effects of this substance upon different kinds of food. Our knowledge of digestion as elucidated further by Hunter, Cruikshank, Magendie, Voit and many others is based almost exclusively upon the results derived from patient and persevering experimentation on animals which have succeeded in solving the problems of digestion, absorption and nutrition, until this part of physiology has reached an enviable degree of perfection. The physiology of the nervous system furnishes one of the strongest and most convincing claims in favor of the indispensable value of experimental research.

Galen gave public demonstrations illustrating the effects of injuries to the cerebro-spinal centres in animals. He divided the spinal cord in the cervical region and showed how this procedure affected the respiratory and other movements. He also studied carefully the phenomena following section of the cord in other places, and, by comparing the different results, obtained a fair knowledge relating to the more important functions of this nervous centre.

From this time little or no progress was made until Sir Charles Bell, Magendie and Mueller again resorted to improved methods of experimentation to throw more light upon this important subject. The motor function of the anterior roots of the spinal nerves was clearly pointed out by Bell in a few carefully conducted experiments and his views were subsequently confirmed and elaborated by Magendie. The numerous and accu-

rate experiments made by Mueller upon the anterior and posterior roots of the spinal nerves in frogs lead to accurate conclusions as to the more important functions of the spinal cord.

Marshall Hall discovered the reflex function of the nervous system and persistently and enthusiastically demonstrated the correctness of his views by experiments on animals.

In our own day, a group of distinguished and faithful investigators, among them Westphal, Ferrier, Hitzig and the lamented Gudden, have been patiently studying the difficult subject of cerebral localization, and the result of their labors has paved the way for successful surgical treatment of a number of lesions of the brain and its envelopes which heretofore invariably resulted in a fatal termination. Muscular contraction was attributed by Galen and his followers to the brain and the spinal cord. This idea was based upon the results of his experiments as he invariably produced muscular paralysis below the point of section of the spinal cord. Haller by his ingenious experiments showed the fallacy of this doctrine which had been handed down from generation to generation as an undisputed fact by demonstrating the existence of an inherent irritablity of the muscular fibre, entirely separate and distinct, of the nervous system.

I might proceed and enumerate countless instances where the results of experimental research have directly or indirectly contributed to the growth and development of the science of physiology, but you must have been convinced by this time that modern physiology consists of a systematic arrangement of facts derived almost exclusively from experimentation. Future advances in physiology can only be realized through the labors of patient and careful experimenters.

The value of experimental research from a practical standpoint becomes more apparent when we contemplate the achievements of modern surgery. The effects of the different anæsthetics had to be carefully determined on animals before it was deemed prudent and safe to apply them in practice. Subcutaneous injections of anodynes were used in the laboratories for years with a view of preventing pain before this prompt and reliable method of relieving pain found its way into general practice.

Artificial respiration was practiced upon animals by Vesalius, Hooke, Lower and others, as a means of prolonging life, long before it was applied to the resuscitation of human beings. Transfusion, as a life-saving operation, is based entirely upon the results derived from experimentation, and can be resorted to as a reliable measure in cases of sudden dangerous loss of blood, a procedure which so far has saved more than half the cases in which it has been attempted. Brown-Sequard has shown that in cases of poisoning with carbonic oxide gas this substance makes a more stable compound with the coloring material of the blood, which incapacitates the red corpuscles from mixing with oxygen, so that in grave cases of this kind this surgical resource constitutes the only possible chance of saving life. Quite recently numerous experiments have been made on animals to test the influence of intravenous infundations of saline solutions in the treatment of acute anæmia as first advocated by Schwarz, and the encouraging results which have been attained have placed this simple and effective procedure upon the list of well-established legitimate surgical resources.

The subject of callus production, regeneration and growth of bone has been made almost exclusively on the lower animals, and this part of surgical pathol-

ogy is intimately associated with the names of Duhamel, Sir Astley Cooper, Ollier, Maas, Busch, Wolff, and our own Brainard. The results of these experiments have opened a wide field for conservative surgery which has resulted in the saving of thousands of useful limbs by the substitution of sub-periosteal resection for the too frequent resort to mutilating operations. Only a few years ago acute suppurative osteomyelitis constituted a subject about which but little was known. To-day, thanks to the patient labors of Kocher, Rosenbach and Ogston, it furnishes the most striking topic of the great value of experimental research. For years surgeons have dreaded to expose the medullary tissue in bone-operations for fear of producing osteomyelitis and the disastrous consequences following it,—thrombo-phlebitis, pyæmia and septicæmia.

Experiments have shown that the myeloid tissue in bone can be torn, contused, crushed, burned, cauterized and the subsequent inflammation will invariably assume a plastic type, provided infection is prevented. On the other hand, it has been found that in animals previously infected with pus-microbes, injury to the medullary tissue is almost invariably followed by suppurative osteomyelitis at the seat of traumatism. We are therefore forced to assume that the floating germs, which might have remained inert for an indefinite period of time, find at the seat of traumatism favorable conditions for localization and reproduction, and are the essential and direct cause of the suppurative inflamation.

That common and heretofore obscure disease, rachitis, has been made an object of patient experimentation by Kassowitz, who has shown that the disease can be artificially produced in animals by the administration of large doses of phosphorus, which causes increased vascularity of bone and *osteo-porosis;* on the other hand the same author has demonstrated that the prolonged administration of minute doses produce an opposite, a curative effect. Numerous practitioners have applied the results of these observations in practice and the majority of them agree with Kassowitz that minute doses of phosphorus constitute almost a specific in the treatment of rachitis. Hagenbach reports twenty consecutive cases treated successfully by this method.

Koch's great discovery of the cause of tuberculosis has revolutionized the treatment of numerous affections which were formerly described under the vague term of scrofula but which are now known to be tubercular in their origin and in their tendencies. The familiar manifestations of so-called scrofula in children, chronic lymphadenitis, tumor albus, and fungous disease of bone, and lupus in the adult, are now well recognized tubercular lesions. In all of these affections the essential primary cause, the bacillus of tuberculosis has been found so constantly that the direct relationship between cause and effect admits of no further argument. But not only the germ has been found in almost every instance but it has been isolated and cultivated upon an artificial soil, and animals infected with the new growth have furnished the crucial test of the tubercular nature of the lesion—reproduction of the same condition histologically, pathologically and clinically. Recognizing the danger arising from local dissemination and generalization through the vascular system, modern surgeons are unanimous in adopting early and thorough local measures, with a firm belief that by a complete removal of the local product, the patient is protected against embolic tuberculosis from the local deposit.

Subcutaneous surgery has only been carried on in a scientific manner and with successful results since the repair of tendons after subcutaneous division was studied on animals by Hunter, Stromeyer, Von Ammon, Bouvier, Guerin and others.

The healing of wounds was made an object of careful experimentation by Hunter, Thiersch and Gussenbauer, and the scientific and practical information thus gained has been of great value in the advancement of surgery. Suturing of divided nerves has become an established practice since the publication of the results of their experimental work by Gluck and Wolberg. An experimental study of cicatrization in blood vessels after ligature, by Jones, Travers, Porta, Hunter, Zwicky, Weber and more recent authors, has gradually led to accurate and correct ideas concerning the immediate action of the ligature and the processes which are initiated, destined to effect definitive obliteration of the lumen of the vessel.

Lister's experiments upon the use of the catgut ligature have led to practical results which alone would constitute a monument which will render the name of the greatest of living surgeons immortal wherever surgery is practiced. Brown-Sequard studied, experimentally, how long the tissues can be left completely deprived of blood without risk of gangrene, observations which led to the use of Esmarch's great invention, substitution of the elastic constrictor for the ordinary imperfect tourniquet in the prevention and arrest of hemorrhage.

Wound fever was studied experimentally, by Lee, Bennet, Pasteur, Colin, Toussaint, Weber, Breuer, Chroback, Bergmann and Koch. The researches of these men prepared the way to antiseptic surgery as first taught and practiced by Lister. The value and importance of the antiseptic treatment of wounds is now almost universally accepted, as the fundamental principles upon which it rests are no longer theories but facts abundantly substantiated by experimental research.

The ætiology, pathology and morbid anatomy of thrombosis and embolism could only be solved by patient and persevering experimentation by such able investigators as Virchow and Panum. Pyæmia and septicæmia, the surgeon's greatest enemies in the pre-antiseptic times, have been carefully studied by experimenters, and we have every reason to hope that work in the same direction in the near future will reveal the true pathology and relationships of these, the most important of all wound infective diseases.

Experiments on dogs made by Winiwarter with a view to determine the feasibility of operative measures upon the stomach, has resulted in the establishment of pylorectomy by Billroth, which has established the practical application of the knowledge thus gained; and a long series of cases, which, if they have not resulted in adding much to the duration of life, demonstrate the justifiability of a resort to the knife in well selected cases.

The history of intestinal surgery is intimately associated with experimental research, and the names of Jobert, Gross and Parks will always be remembered in connection with this department of surgery. Before Simon ventured to resort to nephrectomy in man he studied the effect of this operation upon animals. As a result of these observations extirpation of the kidney is now a well established operation and has already gained a legitimate sphere in cases heretofore abandoned to certain death. The results of extirpation of the spleen in animals has satisfied surgeons that this organ can be removed with safety and a fair prospect

of success in cases of injury or local disease.

The most remote abdominal organ, the pancreas, has been submitted to experimental investigation, and the results thus obtained have shown the feasibility and justifiability of surgical interference in a number of well defined lesions. Experiments upon the liver of animals have shown the necessity of resorting to local measures in arresting hemorrhage where this organ is injured, and o securing a condition for the visceral wound which will favor the healing process, and, at the same time, prevent the disastrous consequences resulting from escape of bile and wound secretions into the peritoneal cavity.

Desault, Albers, Koeberle and Hueter advocated the propriety of extirpation of the larynx, but the advisability of this operation had to be tested by Czerny upon dogs before surgeons could be induced to adopt it as a legitimate surgical procedure. Within a few years 96 extirpations of the larynx have been made, with 32 cures and 64 deaths, a satisfactory showing when we consider that without it all of these patients were doomed to die a horrible death from asphyxia.

Successful extirpations of portions of the lung in animals by Gluck and Schmid have encouraged surgeons to attack this important organ (in well selected cases), when the seat of localized lesions, and in corroboration of the value of these experiments I will only refer to the successful case of Kroenlein, who extirpated a piece of sarcomatous lung with a portion of the chest-wall, and the patient not only recovered from the operation but was reported in good health and without any indications of a return of the disease after two years.

I have only enumerated a number of the most convincing illustrations of the value of experimental research to the practice of surgery, but enough has been said to substantiate the assertion that it is the foundation of modern surgery. It would be difficult to point out pathological conditions or operative measures which do not show the impress and great value of this method of investigation. The recent rapid advances in surgery are entirely owing to original experimental work. German surgery leads the world, because the leading surgeons of that country are original investigators.

If the brilliant achievements of modern surgery are the direct outcome of experimental research, it requires no argument to show that future improvements will depend upon the same method of investigation. The American profession has as yet not realized the importance of original work. Instead of borrowers we must become producers.

I can give you no better advice on this occasion than to devote your leisure moments, from the very beginning of your professional career, to original work of this kind. The means for such an undertaking may be limited, but perseverance will overcome difficulties. Your efforts will be appreciated and your alma mater will look with pride upon the results of your labors. Your colleagues will esteem your motives to promote science and your work will command the respect of the entire profession. Another great advantage only to be acquired by operations upon animals is dexterity in the use of instruments and delicacy of manipulation in the performance of difficult operations. Visceral surgery can only be learned in this manner. Operations upon the gastro-intestinal canal should invariably be practiced upon animals before attempting it on man. A course in operative surgery on the cadaver is utterly inadequate to prepare a student

sufficiently to perform gastrotomy, intestinal resection, or even apply intestinal sutures with requisite speed and accuracy. Proficiency in abdominal surgery can only be acquired by operating upon living tissues. Ligation of arteries in their continuities, again, is another operation in the technique of which you can only perfect yourselves by practicing upon animals. It must have become apparent to you that in order to succeed as scientific men you are not to lead a life of leisure.

If in the beginning of your practice time hangs heavy and patients come slowly, do not become discouraged. Utilize every moment of your time to prepare yourselves the better for your work. Identify yourselves with the local medical societies and take an active part in the scientific work. Keep abreast with the advances in medical science by reading and studying the best literature. Take an active part in preventive medicine, and act as guardians of public health. Become at once original investigators. If you do all these things you will have no just cause of complaint of a surplus of time, or to seek places of idle amusement. The laboratory, the books, the journals, the microscope, the medical societies will become your most devoted and truest friends. When the curtain shall drop behind the scene of a busy, well spent life, a coming grateful generation will inscribe your names upon the walls of the temple of science which you have helped to erect. In bidding you an affectionate farewell I will give you the watchword that will secure your entrance into the ranks of successful men:—*work*, *uninterrupted*, *hard*, *faithful*, *honest work*.